

SUPPLEMENTAL AMENDMENT & RESPONSE UNDER

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Serial No.: 09/634207

Filed: August 9, 2000

Title: INDOLE COMPOUNDS USEFUL FOR THE TREATMENT OF CANCER

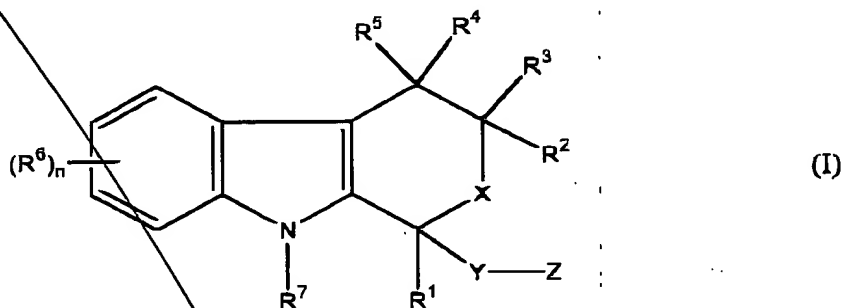
IN THE CLAIMS

Please amend the claims as follows:

Please ass claim 49, amend claims 10, 12, 13, 14, 15, 17, 18, and 19 and cancel claim 11 without prejudice. Applicants reserve the right to pursue the cancelled subject matter in a continuing application.

Claims 1-9 (Cancelled).

Please enter
~~10.~~ (Previously Amended) A method of ~~inhibiting the viability of~~ treating leukemia, multiple myeloma or prostate cancer cells in a mammal comprising administering an effective amount of a compound of formula (I):



Sub E1

wherein R^1 is lower alkyl, lower alkenyl, (hydroxy)lower alkyl, lower alkynyl, phenyl, benzyl or 2-thienyl, R^2 , R^3 , R^4 and R^5 are the same or different and are each hydrogen or lower alkyl; each R^6 is individually hydrogen, lower alkyl, hydroxy, (hydroxy)lower alkyl, lower alkoxy, benzyloxy, lower alkanoyloxy, nitro or halo, n is 1-3, R^7 is hydrogen, lower alkyl or lower alkenyl, X is oxy or thio, Y is carbonyl, $(CH_2)_{1-3}$, $(CH_2)_{1-3}SO_2$ or $(CH_2)_{1-3}C(O)$, and Z is $(\omega-(4\text{-pyridyl}))(C_2\text{-}C_4\text{alkoxy})$, $(\omega-(R^8)(R^9)\text{ amino})(C_2\text{-}C_4\text{ alkoxy})$, wherein R^8 and R^9 are each H, $(C_1\text{-}C_3)\text{alkyl}$ or, together with N, are a 5- or 6-membered heterocyclic ring having 1-3 N(R^8), S or nonperoxide O; an amino acid ester of $(\omega-(HO)(C_2\text{-}C_4))\text{alkoxy}$, $N(R^8)CH(R^8)CO_2H$, 1'-D-glucuronyloxy, OH, $(C_2\text{-}C_4)\text{acyloxy}$, SO_3H , PO_4H_2 , $N(NO)(OH)$, SO_2NH_2 , $PO(OH)(NH_2)$, $OCH_2CH_2N(CH_3)_3^+$,

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Sub
E1
C1

amino, lower alkylamino, di(lower alkyl)amino, phenylamino, or tetrazolyl; or a pharmaceutically acceptable salt thereof; to a mammal afflicted with leukemia, multiple myeloma or prostate cancer.

11. (Cancelled)

Sub
E1

2
12. (Amended) The method of claim ~~10~~¹ or ~~11~~ wherein the treatment is for cancer is prostate cancer.

Sub
E1

3
13. (Amended) The method of claim ~~10~~¹ or ~~11~~ wherein the treatment is for cancer is multiple myeloma.

D
A

4
14. (Amended) The method of claim ~~10~~¹ or ~~11~~ wherein the treatment is for ^{leukemia} cancer is chronic lymphocytic leukemia.

D
A

5
15. (Amended) The method of claim ~~10~~¹ or ~~11~~ wherein the ^{compound} composition is administered orally.

6
16. (Original) The method of claim ~~15~~⁵ wherein an enterically coated dosage form is administered.

7
17. (Amended) The method of claim ~~10~~¹ or ~~11~~ wherein the compound of formula (I) ~~composition~~ is administered parenterally.

8
18. (Amended) The method of claim ~~10~~¹ or ~~11~~ wherein the compound of formula (I) ~~composition~~ is administered in combination with a chemotherapeutic agent.

9
19. (Amended) The method of claim ~~12~~² wherein the compound of formula (I) ~~composition~~ is administered in combination with a chemotherapeutic agent.

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C

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¹⁰
~~20.~~ (Previously Amended) The method of claim ~~18~~⁸ wherein the chemotherapeutic agent is mitoxantrone, prednisone, estramustine, melphalan, vinblastine or a combination thereof.

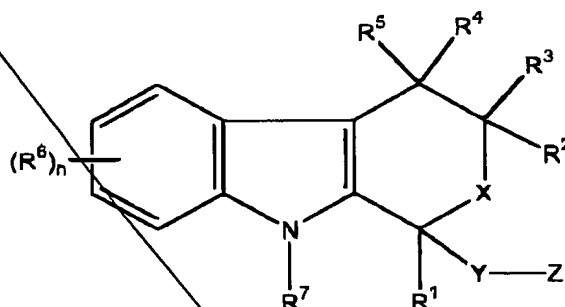
¹¹
~~21.~~ (Previously Amended) The method of claim ~~19~~⁹ wherein the chemotherapeutic agent is an anti-androgen.

¹²
~~22.~~ The method of claim ~~21~~¹¹ wherein the anti-androgen is bicaftamide, nilutamide, flutamide, cycloproterone acetate or a combination thereof.

¹³
~~23.~~ The method of claim ~~21~~¹¹ wherein the anti-androgen is leuprolide acetate, goserelin acetate or a combination thereof.

Claims 24-48 (Cancelled).

¹⁴
~~49.~~ (New) A method of treating hematopoietic cancers, cancers of the bone marrow, [cancers of the colon], and cancers that express high levels of PPAR- γ in a mammal comprising administering an effective amount of a compound of formula (I):



(I)

wherein R¹ is lower alkyl, lower alkenyl, (hydroxy)lower alkyl, lower alkynyl, phenyl, benzyl or 2-thienyl, R², R³, R⁴ and R⁵ are the same or different and are each hydrogen or lower alkyl; each R⁶ is individually hydrogen, lower alkyl, hydroxy, (hydroxy)lower alkyl, lower alkoxy, benzyloxy, lower alkanoyloxy, nitro or halo, n is 1-3, R⁷ is

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hydrogen, lower alkyl or lower alkenyl, X is oxy or thio, Y is carbonyl, $(CH_2)_{1-3}$, $(CH_2)_{1-3}SO_2$ or $(CH_2)_{1-3}C(O)$, and Z is $(\omega-(4\text{-pyridyl})(C_2\text{-}C_4\text{alkoxy}), (\omega-((R^8)(R^9) \text{ amino})(C_2\text{-}C_4\text{alkoxy}),$ wherein R^8 and R^9 are each H, $(C_1\text{-}C_3)\text{alkyl}$ or, together with N, are a 5- or 6-membered heterocyclic ring having 1-3 $N(R^8)$, S or nonperoxide O; an amino acid ester of $(\omega-(HO)(C_2\text{-}C_4))\text{alkoxy}$, $N(R^8)CH(R^8)CO_2H$, 1'-D-glucuronyloxy, OH, $(C_2\text{-}C_4)\text{acyloxy}$, SO_3H , PO_4H_2 , $N(NO)(OH)$, SO_2NH_2 , $PO(OH)(NH_2)$, $OCH_2CH_2N(CH_3)_3^+$, amino, lower alkylamino, di(lower alkyl)amino, phenylamino, or tetrazolyl; or a pharmaceutically acceptable salt thereof; to a mammal afflicted with hematopoietic cancer, cancer of the bone marrow, cancer of the colon, and cancer that expresses a high level of PPAR- γ .
